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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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10/823,647

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11/03/2006

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EXAMINER

KIM, TAEYOON

ART UNIT

PAPER NUMBER

1651

DATE MAILED: 11/03/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

<b>Office Action Summary</b>	<b>Application No.</b> 10/823,647	<b>Applicant(s)</b> THIRUVENGADAM ET AL.	
	<b>Examiner</b> Taeyoon Kim	<b>Art Unit</b> 1651	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --  
**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

#### Status

- 1) ☒ Responsive to communication(s) filed on 05 October 2006.  
 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.  
 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

#### Disposition of Claims

- 4) ☒ Claim(s) 1-34, 38, 44-46 & 48-51 is/are pending in the application.  
 4a) Of the above claim(s) 1-26, 33, 34, 38, 44, 46 and 48-51 is/are withdrawn from consideration.  
 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.  
 6) ☒ Claim(s) 27-32 & 45 is/are rejected.  
 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.  
 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

#### Application Papers

- 9) ☐ The specification is objected to by the Examiner.  
 10) ☒ The drawing(s) filed on 14 April 2004 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.  
 Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
 Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).  
 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

#### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).  
 a) ☐ All b) ☐ Some \* c) ☐ None of:  
 1. ☐ Certified copies of the priority documents have been received.  
 2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.  
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

#### Attachment(s)

- |  |   |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)                                | 4) <input type="checkbox"/> Interview Summary (PTO-413)<br>Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)                       | 5) <input type="checkbox"/> Notice of Informal Patent Application                       |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)<br>Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____  |

### **DETAILED ACTION**

Claims 1-34, 38, 44-46 and 48-51 are pending.

#### ***Election/Restrictions***

Applicant's election without traverse of Group II (claims 27-32 and 45) and ethacrynate as the species elected in the reply filed on Oct. 5, 2006 is acknowledged.

Claims 35-37, 39-43 and 47 have been cancelled, 1-26, 33, 34, 38, 44, 46 and 48-51 have been withdrawn from consideration as being drawn to non-elected subject matter. Claims 27-32 and 45 have been considered on the merits.

#### ***Priority***

Applicant's claim for the benefit of a prior-filed application under 35 U.S.C. 119(e) or under 35 U.S.C. 120, 121, or 365(c) is acknowledged. Applicant has not complied with one or more conditions for receiving the benefit of an earlier filing date under 35 U.S.C. 119(e) as follows:

The later-filed application must be an application for a patent for an invention which is also disclosed in the prior application (the parent or original nonprovisional application or provisional application). The disclosure of the invention in the parent application and in the later-filed application must be sufficient to comply with the requirements of the first paragraph of 35 U.S.C. 112. See *Transco Products, Inc. v. Performance Contracting, Inc.*, 38 F.3d 551, 32 USPQ2d 1077 (Fed. Cir. 1994).

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The disclosure of the prior-filed application, Application No. 60/515,846, fails to provide adequate support or enablement in the manner provided by the first paragraph of 35 U.S.C. 112 for one or more claims of this application. Claims 27-32 and 45 of the current application are not supported by '846 application because there is not steps of the method described in '846 application. For example, there is no disclosure of "a bipolar control" in '846 application. Furthermore, the limitation of claim 30 is not disclosed in '846 application. Therefore, the priority based on '846 application has not been granted.

***Claim Rejections - 35 USC § 112***

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 27-32 and 45 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement and the written description requirement. The claims contain subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. The claims also contain subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The factors to be considered in determining whether undue experimentation is required are summarized in *In re Wands*, 858 F.2d 731, 737, 8 USPQd 1400, 1404 (Fed. Cir. 1988) (a) the breadth of the claims; (b) the nature of the invention; (c) the state of the prior art; (d) the level of one of ordinary skill; (e) the level of predictability in the art; (f) the amount of direction provided by the inventor; (g) the existence of working examples; and (h) the quantity of experimentation needed to make or use the invention based on the content of the disclosure. While all of these factors are considered, a sufficient number are discussed below so as to create a *prima facie* case.

The method of the current claims is based on the assumption that there is a significant difference in membrane potential mediated by sodium pump ( $\text{Na}^+\text{K}^+$  ATPase) between bipolar patients and normal control. However, it is controversial whether the activity of sodium pump for diagnosing bipolar disorder can be used as a reliable basis, evidenced by contradicting results from El-Mallakh et al. (1996) and Buss et al. (1996). Even further, applicant stated in the specification (p. 7, lines 1-9) "one would not expect  $\text{Na}^+\text{K}^+$  ATPase activity to serve as a reliable basis for diagnosing bipolar disorder in an individual patient, because measurements of  $\text{Na}^+\text{K}^+$  ATPase activity are highly variable", and applicant has further disclosed that it is not reliable to use transmembrane potential to serve as a basis of diagnosing bipolar disorder. It is contradicting statement because applicant also disclosed in the specification (p. 8, lines 9-13) that they found the membrane potential in cultured cells from bipolar patients is significantly different than the membrane potential in cultured cells from unaffected controls and siblings. Therefore, based on these contradicting evidences from

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applicant's own disclosures and the prior art references, the method of the current claims would not have a reasonable expectation for a person of ordinary skill in the art at the time of invention made to use for diagnosis of bipolar disorder. In addition, it is difficult to know whether bipolar control patients who would be diagnosed based on the clinical interviews and examination using the Diagnostic and Statistical Manual of Mental Disorders (DSM-IV) indeed have bipolar disorder, because of well-known misdiagnosis problems.

Furthermore, the measurement of membrane potential in cells from unaffected control individuals would be difficult without knowing the activity of sodium pump in those particular individuals. It would be expected that under the various different physiological conditions other than bipolar disorder, one would have altered activity of  $\text{Na}^+\text{K}^+$  ATPases and hence having altered membrane potential. For example, it has been shown that people with migraine appears to have no activity of sodium pump due to a mutation in sodium pump gene as shown by De Fusco et al. (2003). Therefore, the activity of sodium pump would change without any indication of bipolar disorder, thus making the method not enabled for diagnosis of bipolar disorder. Further, there is no full, clear, concise, and exact description in the specification how to select the control (negative) and the bipolar control (positive) patients to obviate such problems.

In addition, according to claim 30, the ratio of membrane potential of cells is obtained by the following way. However, this is not described in the specification.

Mean membrane potential of cells of the patient  
incubated in the absence of  $K^+$  and in the presence  
of a compound that alters  $Na^+K^+$  ATPase activity

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Mean membrane potential of cells of the patient  
incubated in the presence of  $K^+$  and in the absence  
of a compound that alters  $Na^+K^+$  ATPase activity

Claims 27-32 and 45 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for blood cells and other cells easily accessible or obtainable from patients, does not reasonably provide enablement for other types of cells which are difficult or impossible to collect from the patients, and cells in vivo. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims. In order to use the method of the current application to diagnose bipolar disorder, it is necessary for a person of ordinary skill in the art to be able to obtain cells from patients and maintain in culture for measuring membrane potentials. Although cells such as blood cells are easily obtainable from patients, other cells such as nerve cells from brain, somatosensory/somatomotoric neurons such as sciatic nerve, or adult stem cells such as hemangioblast from bone marrow are extremely difficult, if not impossible, to isolate from patients and to grow them in culture as supported by an article entitled Cloning: Present Uses and Promises (see 1<sup>st</sup> line of p.3; <http://ospp.od.nih.gov/policy/cloning.asp>). The specification does not teach how to obtain such cells for a person of ordinary skill in the art in order to use the method of the

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current application, and hence a person of ordinary skill in the art would not have a reasonable expectation to use the method of the current invention.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 27-32 and 45 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

In these claims, the term "a patient" is not clearly pointing out and distinctly claiming the subject matter. It appears that the term "a patient" points out a human patient. Since it would also be possible that the patient is a non-human animal.

The term "cells" in the claims is not clear whether they are cells in vivo or cells in culture (in vitro or ex vivo) isolated from a certain tissue. It appears that the cells are isolated from the patient. However, it is not clearly pointed out in the claims. In addition, there is no active step claimed in the method of current application how to obtain cells from a patient.

The terms "significantly" and "significant" in claim 27 and its dependents is a relative term which renders the claim indefinite. The term "significantly" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably appraised of the scope of the invention.



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The term "bipolar I disorder" in claim 45 does not clearly point out and distinctly claim the subject matter. There is no description on this term in the specification.

The phrase "...one or more people known to (not) have said bipolar..." does not clearly point out the subject matter. It is not clear whether one or more people diagnosed by DSM-IV or other means of diagnosis.

### ***Conclusion***

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Taeyoon Kim whose telephone number is 571-272-9041. The examiner can normally be reached on 8:00 am - 4:30 pm ET (Mon-Fri).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Wityshyn can be reached on 571-272-0926. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a

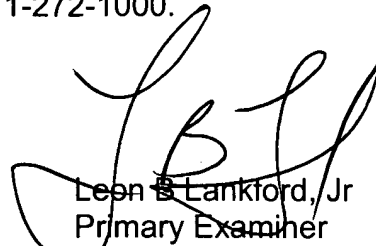
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